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Sitting time, physical fitness impairments and metabolic abnormalities in people with bipolar disorder:  
an exploratory study

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## Abstract

A sedentary lifestyle is an independent risk factor for cardiovascular disease and mortality. Little is known however about sedentary behavior in people with bipolar disorder (BD). The primary aim of this study was to explore associations between sitting time (as a proxy for a sedentary lifestyle) and physical fitness and metabolic parameters in BD. A secondary aim was to investigate associations between psychiatric symptoms, psychotropic medication use and sitting time. Thirty-nine (21♀) participants (43.7±12.4 years) completed a full metabolic screening, the sitting time item of the International Physical Activity Questionnaire, the Quick Inventory of Depressive Symptomatology self-

report and the Hypomania Checklist-32. Additionally participants performed the Eurofit-test battery and 6-minute walk test. The mean time spent sitting per day for the entire sample was  $7.0 \pm 3.0$  hours. A higher body mass index, worse physical fitness and higher antipsychotic medication dose were identified as independent predictors of higher levels of sitting behaviour. The model explained 76.5% of the variability in the sitting time. Given that a sedentary lifestyle is an independent predictor of cardiovascular disease, future interventions specifically targeting time spend sitting are warranted in BD, with a particular emphasis on those with high body mass index and low fitness levels.

**Keywords:** bipolar disorder; depression; sitting; exercise; metabolic syndrome; physical fitness

## Introduction

A recent meta-analysis (Walker et al., 2015) demonstrated that mortality rates are approximately two to three times higher in people with bipolar disorder than those of the general population. The higher premature mortality rates are largely attributable to cardiovascular disease (Goldstein et al., 2015). In the general population there is evidence that physical activity and exercise are broadly as effective as pharmacological interventions in preventing cardio-metabolic diseases and consequently premature mortality (Naci and Ioannidis, 2013). Data in people with bipolar disorder are however inconsistent with some studies finding a strong association between the level of physical activity participation and the risk for cardio-metabolic diseases (Salvi et al., 2011), while others in a mixed study including people with bipolar disorder and schizophrenia did not (Bly et al., 2014). Physical activity guidelines and recommendations for preventing and treating cardiovascular diseases have historically emphasized moderate-vigorous physical activity, or physical activity at an intensity greater than 45% of the maximum oxygen uptake (Garber et al., 2011). In last years, there has been a rapid emergence of studies indicating that cardiovascular disease risks are also, independent of the physical activity behavior, associated with sedentary behavior (Wilmot et al., 2012). Sedentary behavior can be defined as an energy expenditure  $\leq 1.5$  metabolic equivalents of task (METs), while in a sitting or reclining posture during waking hours (Cart, 2012). To date, there is a paucity of data on sedentary behavior among people with bipolar disorder. In an exploratory study among 60 adult outpatients with bipolar

disorder, patients were sedentary for approximately 13.5h per day according to accelerometers worn over seven consecutive days (Janney et al., 2014). This is more than double the level of sedentary behavior reported in older populations (>60 years) (mean=5.3h per day) (Harvey et al., 2014) and similar to the levels found in people with psychosis (Stubbs et al., 2016). The extent to which sedentary behavior in people with bipolar disorder contributes to the previously observed physical fitness impairments (Vancampfort et al., 2015c; Vancampfort et al., 2015e) and metabolic abnormalities (Vancampfort et al., 2015d), both predictors for cardiovascular diseases and premature mortality (Lee et al., 2010), is unknown. Given that sedentary behavior is modifiable, understanding sedentary behavior levels and correlates might offer a unique opportunity to reduce the considerable cardio-metabolic rates seen in people with bipolar disorder (Vancampfort et al., 2015a; Vancampfort et al., 2013).

The primary aim of this cross-sectional study was to explore associations between sitting time, as the most common sedentary behavior, and physical fitness and metabolic parameters in people with bipolar disorder. A secondary aim was to investigate associations between sitting time and psychiatric symptoms and psychotropic medication use.

## Methods

### *Participants and procedure*

Over a 6-month period, inpatients with a DSM-5 diagnosis of bipolar disorder (American Psychiatric Association, 2013) of the University Psychiatric Center KU Leuven campus Kortenberg in Belgium were invited to participate. Since severe substance abuse might impair the physical fitness test performances (Herbsleb et al., 2013), participants were excluded if they had a co-morbid DSM-5 diagnosis of substance abuse during the previous 6 months. The somatic exclusion criteria included evidence of significant cardiovascular, neuromuscular and endocrine disorders which, according to the American College of Sports Medicine (2009) might prevent safe participation in the study. All participants received a physical examination and baseline electrocardiogram before testing. All participants completed first a full metabolic screening. Afterwards they completed the sitting time item of the International Physical Activity Questionnaire (Craig et al., 2003), the Quick Inventory of Depressive Symptomatology self-report (Rush et al., 2003) and the Hypomania Checklist-32 (Angst et al., 2005). Additionally they performed the Eurofit test battery (Oja and Tuxworth, 1995) and 6 minute

walk test (6MWT) (ATS, 2002). Participants were requested to refrain from eating, drinking coffee or smoking during a two-hour period prior to the tests. The study procedure was approved by the Scientific and Ethical Committee of the UPC KU Leuven, campus Kortenberg, Belgium and conducted in accordance with the principles of the Declaration of Helsinki. All participants gave their informed written consent. There was no compensation for participation in the study.

#### *Sitting time - International Physical Activity Questionnaire (IPAQ)*

Overall sitting time, a suitable proxy for sedentary behavior, was assessed using the long-version of the IPAQ (Craig et al., 2003) on which participants reported the total time they spent sitting down while doing things like visiting friends, reading, watching television, or working at a desk or computer on a typical weekday and typical weekend day in the last week. Sitting in a motor vehicle was assessed separately. Overall sitting time in this study was calculated as sitting during motorized transportation + [(weekday sitting except for transport \*5) + (weekend day sitting except for transport \*2)/7] and reported in hours per day. The IPAQ has been used previously to assess sitting time in people with serious mental illness (Stubbs et al., 2015b; Vancampfort et al., 2012).

#### *The Eurofit test battery*

The Eurofit test battery (Oja and Tuxworth, 1995) includes 7 items and involves the assessment of the following measures: whole body balance, speed of limb movement, flexibility, explosive strength, static strength, abdominal muscular endurance and running speed.

Whole body balance (flamingo balance) was measured as the number of trials needed by individuals to achieve a total duration of 30sec in balance on their preferred foot on a flat firm surface. While balancing on the preferred foot (shoes removed), the free leg is flexed at the knee and the foot of this leg held close to the buttocks. Lower flamingo balance scores indicate a better whole body balance.

Speed of limb movement (plate tapping) was assessed using a table on which two discs at 80cm distance had to be touched alternately with the preferred hand as fast as possible, completing 25 cycles. Higher scores indicate lower speed of limb movement.

Flexibility was measured using the sit-and-reach test. Participants sat on the floor with straight legs and reached forward as far as possible (shoes removed). The knees were held in extended

position by the investigator throughout the test. The feet were placed against a test box with a ruler placed on the top of the box. The ruler had to be pushed with the fingertips and this in a smooth and slow movement. Higher scores indicate better flexibility.

Explosive strength was measured by a standing broad jump, using a tape measure on a foam mat. Participants were asked to stand behind a line drawn perpendicular to the tape measure and jump forward as far as possible using arm swing and knee bending before jumping. The distance jumped was recorded from the take-off line to the farthest point backward of the participant. Higher scores indicate a better explosive strength.

Handgrip strength was assessed using a handgrip dynamometer (Lafayette Instruments Hand Dynamometer) to be squeezed as forcefully as possible with the preferred arm fully extended slightly away from the body, and palm facing inward. Higher scores indicate better handgrip strength.

Abdominal muscle endurance was measured as the number of correctly completed sit-ups in 30seconds. Sit-ups were performed with the hands placed at the side of the head, knees bent at 90 degrees, and the feet secured by the investigator. A full sit-up is defined as touching the knees with the elbows and returning the shoulders to the ground. A higher number of completed sit-ups indicates greater abdominal muscle endurance.

Running speed was assessed using a 10 by 5m shuttle run. Each participant was required to sprint 10 times between two lines placed 5m apart over a 1.3 m wide track. The sprint was followed by immediately turning and running back. Lower scores indicate better running speed.

Following the manual (Oja and Tuxworth, 1995), except for the flamingo balance test, the sit-ups test and the shuttle run, each test was done twice and the better score was recorded. Supervision and measurement of the Eurofit test battery was performed by one trained mental health physical therapist.

#### *The 6 minute walk test (6MWT)*

The 6MWT was performed according to the American Thoracic Society guidelines in an indoor hallway with a minimum of external stimuli (ATS, 2002). Two cones 25m apart indicated the length of the walkway. Participants were instructed to walk back and forth around the cones during 6 minutes, without running or jogging. Resting was allowed if necessary, but walking was to be resumed as soon as the participants were able to do so. The protocol stated that the testing was to be interrupted if

threatening symptoms appeared, including (a) chest pain, (b) intolerable dyspnea, (c) leg cramps, (d) staggering, (e) diaphoresis, and (f) pale or ashen appearance. The total distance walked in 6 minutes was recorded to the nearest decimetre. Standardised encouragements were provided at recommended intervals. All supervisions and measurements of the 6MWT were performed by the same mental health physical therapist.

#### *Quick Inventory of Depressive Symptomatology self-report (QIDS -SR)*

QIDS-SR (Rush et al., 2003) consists of 16 items each ranging from 0 to 3. Scores range from 0 to 27 with higher scores indicative for higher symptom severity. The QIDS-SR is a standardized measure of depressive symptoms and has demonstrated adequate psychometric validity in patients with bipolar disorder (Trivedi et al., 2004).

#### *Hypomania Checklist - 32 (HCL-32)*

The HCL-32 (Angst et al., 2005) consists of 32 yes/no statements regarding a period when the patient remembers he was in a “high” mood. Items ask whether specific behaviors (e.g., “I spend more money/too much money”), thoughts (e.g., “I think faster”), or emotions (e.g., “my mood is significantly better”) were present in such a state. Scores range from 0 to 32. Higher scores reflect more severe hypomanic states. The HCL-32 has been cross-culturally validated; also in a Belgian subsample (Angst et al., 2010).

#### *Smoking behavior*

Participants were asked whether they smoked or not, and if so, how many cigarettes they smoke per day on average.

#### *Metabolic screening*

All patients underwent a fasting metabolic screening. The presence of MetS was assessed using the International Diabetes Federation criteria (Alberti et al., 2005). Body weight was measured in light clothing to the nearest 0.1kg using a SECA beam balance scale, and height to the nearest 0.1cm using a wall-mounted stadiometer.



*Medication use*

We recorded the use of antipsychotic medication, antidepressants, and mood stabilizers. Antipsychotic medication was recorded and converted into a daily equivalent dosage of chlorpromazine (Gardner et al., 2010). Mean dosages of specific mood stabilizers and antidepressants were reported when they were used by at least 10 participants.

*Statistical analyses*

Data were assessed for normality using the Shapiro-Wilk test, with all data found to have a normal distribution. Descriptive statistics are therefore presented as mean  $\pm$  standard deviation (SD). Unpaired t-tests were used to examine the difference in sitting time between patients and healthy controls. Relationships between variables were calculated using the Pearson correlation coefficients. A backward stepwise regression analysis was performed to evaluate independent variables explaining the variance in sitting time. To prevent overfitting of the models, only variables significant ( $P < 0.05$ ) in the univariate analyses were entered into the final model. To test for multicollinearity, a variance inflation factor (VIF) was computed for each independent variable in the model. Values above 3 were used to indicate a multicollinearity problem in the model (Kleinbaum et al., 2013). If we encountered a VIF above 3 between two independent variables, we only included the independent variable with the strongest correlation coefficient with the dependent variable. The significance level was set at  $P < 0.05$ . Statistical analyses were performed using the statistical package SPSS version 22.0 (SPSS Inc., Chicago, IL).

**Results***Participants*

A total of 51 persons with bipolar disorder were initially recruited. Four persons with co-morbid substance abuse during the previous 6 months were excluded. Two persons were excluded as a consequence of a cardiovascular or neuromuscular disorder that might prevent safe participation. Of the 45 included persons with bipolar disorder, 5 declined to participate (i.e. not interested). One patient indicated he could not estimate how much time he spent sitting and was excluded from the analyses.

Thirty-nine (35 with bipolar – I and 4 with bipolar – II disorder) participants were included in the final analysis. Within the final sample 18 men (age=43.9±11.1 years; illness duration=17.5±10.6 years; body mass index, BMI=26.1±3.3) and 21 women (43.5±13.6 years; illness duration=17.4±13.3 years; body mass index, BMI=25.8±4.0) were represented. All participants apart from one were Belgian natives. Sixteen (41.0%) of the participants smoked. The mean time spent sitting per day for the entire sample was 7.0 ± 3.0 hours. Other demographical and clinical variables are presented in Table 1.

#### *Associations of the time spent sitting with demographical and clinical variables*

An overview of the demographical and clinical associations of the time spent sitting is summarized in Table 1. A longer time spent sitting per day was associated ( $P<0.05$ ) with an older age (years), a longer illness duration (years), a higher BMI, a higher antipsychotic medication dose (expressed as chlorpromazine equivalents), a worse whole body balance (flamingo balance), speed of limb movement (plate tapping), explosive strength (standing broad jump), static strength (handgrip strength), abdominal muscular endurance (sit-ups), and running speed (shuttle run) test performance, a lower distance achieved on the 6MWT (m), a higher number of MetS criteria fulfilled (n), a higher waist circumference (cm) and a higher QIDS-SR score. There was no difference in sitting time between men versus women (6.3±2.9 versus 7.7±3.1 hours,  $P=0.18$ ). Patients with MetS ( $n=14$ ) engaged significantly more time sitting than those without MetS (9.2±3.0 versus 5.8±2.4 hours,  $P=0.001$ ).

Insert Table 1 about here

All significant correlates for sitting time per day were included in a backward regression analysis (Table 2). Regarding the MetS parameters, we only included the presence of MetS as an independent variable. Within the fully adjusted model body mass index, the shuttle run performance and the antipsychotic medication dose (expressed as chlorpromazine equivalents) were identified as independent predictors of the time spent sitting. The model explained 76.5% of the variability in the sitting time. There was no multicollinearity among the variables within the final model.

Insert Table 2 about here

## Discussion

### *General findings*

The current study is, to our knowledge, the first to investigate sedentary behavior in people with bipolar disorder. Our data show that a higher BMI, worse physical fitness (shuttle run test performance) and a higher antipsychotic medication dose are associated with a more sedentary lifestyle.

A higher BMI is a measure-of-proxy for the presence of obesity. Obesity consistently emerges as a key and potentially modifiable risk factor in the onset and progression of musculoskeletal conditions and pain (Wearing et al., 2006), which in its turn impairs the ability to perform weight-bearing activities such as walking. Previous research demonstrated that people with bipolar disorder with a higher BMI indeed experience more foot or ankle problems and back pain, which impairs the ability to perform daily life activities (Vancampfort et al., 2015e). The assessment and treatment of such bodily pain should therefore form an integral part of the management of bipolar disorder (Stubbs et al., 2015a). Future interventional research should explore whether addressing bodily pain is an important strategy to reduce sedentary behaviors in this high risk population.

We also found evidence of the MetS being associated with sitting time in our data. Previous research among people with established psychosis (Stubbs et al., 2015b), found that higher levels of sedentary behavior are associated with elevated c-reactive protein. Taken together, our data suggests that sedentary behavior may be associated with increased inflammation, a relationship observed in the general population (Wilmot et al., 2012). It might be postulated that these inflammatory processes may cause pathological microvascular changes that can affect gas transfer across the alveolar-capillary membrane, which in turn may affect the circulatory, respiratory, and muscular systems involved in supplying oxygen to the body (Ostermann et al., 2012). A previous pilot study in patients with schizophrenia already demonstrated that the presence of MetS is associated with an increased prevalence of restrictive lung dysfunction (Vancampfort et al., 2014b), which on its turn might impair the ability to perform physical activities (Vancampfort et al., 2014a). In an additional analysis we did find that the shuttle run test performance in people with MetS was significantly worse than in those without MetS ( $31.2 \pm 7.4$  versus  $25.6 \pm 6.5$ ,  $P=0.027$ ). Our data also suggest that the shuttle run test

performance is associated with a more sedentary lifestyle. Previous large-scale population research demonstrated that in particular among sedentary or lightly physically active persons, inverse associations between total daily sitting time and cardiorespiratory fitness can be found, while there is no such association between sitting time and cardiorespiratory fitness among moderately or vigorously physically active persons (Eriksen et al., 2015).

It might be hypothesised that in people with bipolar disorder exposure to depressive symptoms translates into a poorer physical fitness, which on its turn is associated with a sedentary lifestyle. A reason for the association between feelings of depression and more time spend sitting might be the fact that feelings of depression are associated with a lower self-efficacy and increased negative outcome expectations when having the intention to engage in daily life activities (Krämer et al., 2014). As physical fitness is a modifiable risk factor, and exercise interventions targeting cardiorespiratory fitness have been shown to have a favourable impact in people with severe mental illness independent from changes in body mass index (Vancampfort et al., 2015b), interventions targeting reductions in sedentary behaviour and improvements in physical fitness should be considered.

Finally, the association between a sedentary lifestyle and the antipsychotic medication dose is of interest and warrants further investigation. Several hypotheses could be explored. It might be that the antipsychotic medication dose is a measure-of-proxy for disease severity and people treated with a higher dose may experience more and more severe psychiatric symptoms. The current data show that e.g. the level of depressive symptoms was associated with the time spent sedentary. We however did not investigate the presence of psychotic symptoms or acute mania. It might also be that patients treated with higher antipsychotic medication doses experience more side-effects such as extrapyramidal symptoms and feelings of fatigue, preventing them for being more physically active during the day.

#### *Limitations and future research*

The findings of the present study need to be interpreted with caution because of some methodological limitations. First, the present research used a self-report questionnaire to assess sitting time in volunteers, and hence may underestimate overall sitting time. Previous research in people with psychosis (Stubbs et al., 2016) already demonstrated that objective measurement of sedentary behavior predicts higher levels of sedentariness. Participants in the current study reported sitting

approximately 7 hours per day, whilst total sedentary time (including lying down) was recorded as almost double (13.5 hours) in a recent study utilizing objective measurement (Janney et al., 2014). There is a need for future research to investigate the utility of self-report measures of sedentary behavior (not only restricted to sitting time) in people with bipolar disorder and compare this to the gold standard objective measurements. Nevertheless, there was a high response rate in the patients' group which should prevent serious distortion of the results in these patients due to selection bias. Second, the cross-sectional design limits inference about the direction of causality between overall sitting time, a higher BMI, a worse physical fitness and a higher antipsychotic medication dose. Future studies should prospectively study the associations found. There is also a pressing need to better understand the health outcomes specifically derived from replacing sedentary time with non-fatiguing types of light intensity physical activity potentially achievable in people with mental illness (Vancampfort et al., 2015f; Vancampfort et al., 2015e). Activity at the lower end of the intensity continuum might replace dozens of hours of sedentary time each week. While strong evidence for implementing physical activity is already available for people with psychotic disorders (Firth et al., 2015), people with bipolar disorder are currently an under-researched population with regards to physical activity related interventions. Third, we did not include possible confounding factors such as alcohol and drugs use, socio-economic status, educational level and duration of treatment. Duration of illness might however be perceived as a measure-of-proxy for duration of treatment. Fourth, we were not able to explore specific antipsychotic medications and instead looked at more general chlorpromazine equivalent doses.

Although with limitations, our findings indicate that the multidisciplinary treatment in people with bipolar disorder should include messages on reducing prolonged sitting. Health care professionals should for example support people with bipolar disorder to limit their recreational screen time (watching television, computer use, playing video games, etc.), time spent sitting during motorized transportation, and time spent sitting in the context of friends or family related activities or during community work (e.g. employment, volunteering). In addition to reducing overall sedentary time, prolonged periods of uninterrupted sedentary time should be minimized by increasing sporadic movements during sedentary time. In practice, this may be achieved by taking brief activity breaks to disrupt prolonged periods of sitting or by increasing movements while sitting (Vancampfort et al.,

2015f; Vancampfort et al., 2015e). Future research should explore if such interventions are efficient in people with bipolar disorder.

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## Conflict of interest

None to report.

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**Table 1.** Associations with time spent sitting per day (hours per day) in people with bipolar disorder

Variable	Mean $\pm$ SD	r with time spent sitting (hours per day)	P*
Age (years) (n=39)	43.7 $\pm$ 12.4	0.35	0.029*
Illness duration (years) (n=39)	17.4 $\pm$ 11.9	0.41	0.01*
Body mass index (kg/m <sup>2</sup> ) (n=39)	26.0 $\pm$ 3.6	0.42	0.008*
Cigarettes per day (number) (n=19)	20.7 $\pm$ 14.5	0.45	0.08
Chlorpromazine equivalents (mg/day)	475.9 $\pm$ 290.8	0.42	0.009*
Lithium (mg/day) (n=14)	928.6 $\pm$ 603.4	0.27	0.35
Valproic acid (mg/day) (n=11)	1777.3 $\pm$ 371.7	0.21	0.53
Eurofit test performance (n=39)			
Flamingo balance (n)	14.7 $\pm$ 8.2	0.71	<0.001*
Plate tapping (sec)	16.1 $\pm$ 6.1	0.54	<0.001*
Sit-and-reach test (n)	20.6 $\pm$ 10.4	-0.08	0.64



Standing broad jump (cm)	125.7±50.8	-0.69	<0.001*
Handgrip strength (kg)	37.6±12.8	-0.35	0.027*
Sit-ups (n)	12.5±6.9	-0.61	<0.001*
Shuttle run (sec)	27.6±7.3	0.58	<0.001*
6MWT (m) (n=39)	598.8±130.5	-0.63	<0.001*
Metabolic syndrome criteria (n=39)			
Number of criteria fulfilled (n)	1.8±1.1	0.44	0.005*
Waist circumference (cm)	92.9±9.7	0.43	0.006*
Systolic blood pressure (mmHg)	120.7±9.7	-0.05	0.74
Diastolic blood pressure (mmHg)	78.8±7.3	-0.02	0.92
HDL (mg/dl)	51.4±16.5	0.06	0.73
Triglycerides (mg/dl)	120.8±56.7	-0.008	0.96
Fasting glucose (mg/dl)	89.3±11.2	0.22	0.17
QIDS –SR score (n=39)	7.4±4.9	0.55	<0.001*
HCL-32 score (n=39)	15.7±7.0	-0.08	0.61

\*Significant when  $P < 0.05$ ,  $r$ =Spearman Rho correlation coefficient, 6MWT= 6 minute walk test distance, HDL= High density lipoproteins, QIDS –SR= Quick Inventory of Depressive Symptomatology self-report, HCL-32=Hypomania Checklist – 32.

**Table 2.** Final model of the backward stepwise regression analysis with the mean sitting time per day as dependent variable

Variables <sup>o</sup>	B	SE	$\beta$	t	VIF	P
(Constant)	-11.5	2.6		-4.4		
Body mass index (kg/m <sup>2</sup> )	0.2	0.1	0.2	2.1	1.1	0.047*
Shuttle run (sec)	0.4	0.07	0.7	2.1	1.1	<0.001*
Chlorpromazine equivalents (mg/day)	0.003	0.001	0.3	6.9	1.1	0.011*

\*Significant when  $p < 0.05$ , <sup>o</sup>Only significant correlates in the univariate analyses were included in the model [i.e., age, illness duration, BMI, antipsychotic medication dose, whole body balance (flamingo balance), speed of limb movement (plate tapping), explosive strength (standing broad jump), static strength (handgrip strength), abdominal muscular endurance (sit-ups), running speed (shuttle run), the 6MWT score, the presence of MetS and

the QIDS-SR score],  $B$ =unstandardized coefficient,  $SE$ =standard error,  $\beta$ =standardized coefficient,  $VIF$ = variance inflation factor.

### Highlights

- People with bipolar disorder spend more than 7 hours per day sitting.
- Antipsychotic medication use is associated with more time spent sitting.
- Management of bipolar disorder should include psycho-education about reducing sitting time.